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EXAMINER

GABEL, GAILENE

ART UNIT PAPER NUMBER

1641

DATE MAILED: 05/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|--------------------------------------|--|--|
| Office Action Summary | Application No. 09/492,214 | Applicant(s) STEMMLER ET AL. | |
| | Examiner Gailene R. Gabel | Art Unit 1641 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 February 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3-5, 10-16, 19, 21, 23, 33-36 and 42-44 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 3-5, 10-16, 19, 21, 23, 33-36 and 42-44 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>2/9/05</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Amendment Entry

1. Applicant's amendment and response filed 2/4/05 is acknowledged and has been entered. Claims 2, 6, 7, 9, and 45-59 have been cancelled. Claims 5, 10, 42, and 44 have been amended. Accordingly, claims 3-5, 10-16, 19, 21, 23, 33-36, and 42-44 are pending and are under examination.

Rejections Withdrawn

2. The rejections of claims 2, 6, 7, 9, and 45-59 are now moot in light of Applicant's cancellation of the claims.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 3-5, 10-16, 19, 21, 23, 33-36, and 42-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "at least some" in claim 42 is a relative term which renders the claim indefinite. The term "at least some" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in

Art Unit: 1641

the art would not be reasonably apprised of the scope of the invention. In this case, the recitation of "the quenching substance suppresses *at least some* of the signal" lacks a comparative basis for defining its metes and bounds.

Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 3-5, 10-16, 19, 21, 23, 33-36, and 42-44 are rejected under 35

U.S.C. 112, first paragraph, because the specification,

A) while being enabling for a method for qualitative and quantitative determination of analyte comprising:

1) incubating a sample containing analyte with a labeled competitive substance and a solid phase coated with a quenching substance and having bound thereto, an analyte specific binding partner, to allow the analyte and the labeled competitive substance to competitively bind to the analyte specific binding partner, wherein the quenching substance suppresses the signal from the labeled competitive substance bound to the solid phase,

2) exciting the sample so as to generate signal from unbound labeled competitive substance, and

3) measuring the signal generated only from unbound labeled competitive substance in a defined volume of the liquid phase, thereby quantitatively or qualitatively

Art Unit: 1641

determining the analyte without physically separating unbound and bound labeled competitive substance;

OR

B) while being enabling for a method for qualitative determination of analyte comprising:

1) incubating a sample containing analyte with a labeled competitive substance and a solid phase coated with a quenching substance and having bound thereto, an analyte specific binding partner, to allow the analyte and the labeled competitive substance to competitively bind to the analyte specific binding partner, wherein the quenching substance suppresses at least some of the signal from the labeled competitive substance bound to the solid phase,

2) exciting the sample so as to generate signal from unbound labeled competitive substance, and

3) measuring the signal generated only from unbound labeled competitive substance in a defined volume of the liquid phase, thereby qualitatively determining the analyte without physically separating unbound and bound labeled competitive substance;

does not reasonably provide enablement for qualitative and quantitative determination of signal generated from any and all of the labeled competitive substance contained in both of the solid phase and the liquid phase, which is encompassed by the claimed invention. The specification does not enable any person skilled in the art to

Art Unit: 1641

which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

As set forth in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

The nature of the invention- the invention is directed to a method for quantitative or qualitative determination of an analyte by incubating a sample containing analyte with a labeled competitive substance and a solid phase coated with a quenching substance and having bound thereto, an analyte specific binding partner, to allow the analyte and the labeled competitive substance to competitively bind to the analyte specific binding partner, wherein the quenching substance suppresses the signal from the labeled competitive substance bound to the solid phase, exciting the sample so as to generate signal from unbound labeled competitive substance, and measuring the signal generated only from unbound labeled competitive substance in a defined volume of the liquid phase, thereby quantitatively or qualitatively determining the analyte without physically separating unbound and bound labeled competitive substance. Alternatively, a qualitative determination of the analyte can be obtained using the method when the

Art Unit: 1641

quenching substance suppresses [only] at least some of the signal from the labeled competitive substance bound to the solid phase.

The state of the prior art- the prior art of record fails to disclose a method as recited in claim 42 wherein the bound and unbound labeled competitive substances contained in the mixture are not physically separated when obtaining measurement of unbound labeled competitive substance, to obtain a quantitative or qualitative determination of the analyte.

The predictability or lack thereof in the art- there is no predictability based on the instant specification that the claimed method will work to provide accurate quantitative measure of analyte concentration or qualitative presence of the analyte.

The amount of direction or guidance present- appropriate guidance is provided by the specification for the claimed method to work if the quenching substance is capable of completely suppressing the signal from the labeled competitive substance bound to the solid phase, and the signal is measured only from unbound competitive substance in a defined volume of the liquid phase to quantitatively or qualitatively determine the concentration of the analyte without physically separating unbound and bound labeled reagent. However, the specification fails to provide any guidance to enable the claimed method to function, without physically separating unbound and bound labeled competitive substance, by merely measuring the signal generated from the labeled competitive substance, as claimed.

The presence or absence of working examples- working examples are provided in the specification that show a method for qualitative and quantitative determination of

Art Unit: 1641

analyte comprising incubating a sample containing analyte with a labeled competitive substance and a solid phase coated with a quenching substance and having bound thereto, an analyte specific binding partner, to allow the analyte and the labeled competitive substance to competitively bind to the analyte specific binding partner, wherein the quenching substance suppresses the signal from the labeled competitive substance bound to the solid phase, exciting the sample so as to generate signal from unbound labeled competitive substance, and 3) measuring the signal generated only from unbound labeled competitive substance in a defined volume of the liquid phase, thereby quantitatively or qualitatively determining the analyte without physically separating unbound and bound labeled competitive substance; OR a method for qualitative determination of analyte comprising: incubating a sample containing analyte with a labeled competitive substance and a solid phase coated with a quenching substance and having bound thereto, an analyte specific binding partner, to allow the analyte and the labeled competitive substance to competitively bind to the analyte specific binding partner, wherein the quenching substance suppresses at least some of the signal from the labeled competitive substance bound to the solid phase, exciting the sample so as to generate signal from unbound labeled competitive substance, and measuring the signal generated only from unbound labeled competitive substance in a defined volume of the liquid phase, thereby qualitatively determining the analyte without physically separating unbound and bound labeled competitive substance. There are no working examples that show analogous results by merely measuring the signal generated from the labeled competitive substance, as claimed.

The quantity of experimentation necessary- it would require undue amount of experimentation for the skilled artisan to make and use the method as claimed.

*The relative skill of those in the art-*the level of skill in the art is high.

The breadth of the claims- as recited, the invention is directed to a method for quantitative or qualitative determination of an analyte by incubating a sample containing analyte with a labeled competitive substance and a solid phase coated with a quenching substance and having bound thereto, an analyte specific binding partner, to allow the analyte and the labeled competitive substance to competitively bind to the analyte specific binding partner, wherein the quenching substance suppresses at least some of the signal from the labeled competitive substance bound to the solid phase, exciting the sample so as to generate signal from the labeled competitive substance, and measuring the signal generated from the labeled competitive substance, thereby quantitatively or qualitatively determining the analyte without physically separating unbound and bound labeled competitive substance; without any regard as to how the signal that determines the qualitative and quantitative measure of the analyte can be differentially generated and accurately measured without interference between bound and unbound components, since only at least some of the signal from the labeled competitive substance bound to the solid phase is suppressed by the quenching substance.

In pages 9 and 10 of the disclosure, Applicant provides that in performing the claimed invention for measuring the bound labeled reagent without physically separating unbound and bound labeled reagent, a qualitative and quantitative determination of analyte concentration can be obtained when measurement signal from

Art Unit: 1641

only one of the signal generating phases present which contains bound labeled reagent is obtained by space-staggered measurement, and each individual measurement signal represents the intensity of fluorescence occurring at each position. In a competitive assay as disclosed by Applicant in page 5, after a binding equilibrium sets in, at least one measurement signal can be taken from a volume segment of the liquid phase, in which the signal generated by the solid phase is essentially not taken, and the measurement signal taken from the liquid phase serves for the calculation of the quantity of analyte contained in that phase and ultimately for determination of the quantities of the analyte present in the sample using a previously created calibration curve. To lower the influence of interference effects from label bound to solid phase, Applicant teaches selecting and using a quenching substance such as gold or silver, that is capable of quenching fluorescence obtained when molecules present in a system are excited by a laser, i.e. within a short distance at less than 100 nm. Specifically, the quenching substance should be provided so that radiation of the solid phase is almost completely suppressed so that it is not necessary to carry out spatially staggered taking of at least one measurement signal, and a spot within a volume segment with a diameter of 40 μm or less can be illuminated and the generated signal taken only from the segment is measured (page 9, first full paragraph and page 10, third full paragraph). While the specification exemplifies methods of qualitatively and quantitatively determining analyte by a series of space-staggered measurement of a signal generating phase or a single measurement of a signal of a defined volume segment of the liquid phase, of a mixture containing bound and unbound components, the specification does

Art Unit: 1641

not show any working examples of the instantly claimed method; and it does not provide any teaching that suggests that a quantitative or qualitative determination of an analyte in a sample mixture containing analyte, a labeled competitive substance, and a solid phase coated with a quenching substance having a analyte binding partner bound thereto, wherein the analyte and the labeled competitive substance is allowed to bind to the analyte binding partner, and excited so as to generate signal from the labeled competitive substance, and can be measured as claimed, without physically separating unbound and bound labeled components. While it is not necessary to show working examples for every possible embodiment, there should be sufficient teachings in the specification that would suggest to the skilled artisan that the breadth of the claimed method is enabled. This is not the case in the instant specification.

In view of the teachings of *In re Wands*, 8 USPQ2d 1400, it has been determined that the level of experimentation required to enable the breadth of the claims is undue. It has been set forth above that 1) the experimentation required to enable the claimed method for determining a qualitative or quantitative determination of analyte, would be great as 2) there is no experimental evidence provided that would indicate that the claimed method of measuring analyte would actually work without physically separating unbound and bound labeled reagent; 3) there is no proper guidance that shows that the claimed qualitative and quantitative methods of measuring analyte would work without physically separating unbound and bound labeled components in the instant specification, 4) the nature of the invention is a method for quantitative or qualitative determination of an analyte by incubating a sample containing analyte with a labeled

Art Unit: 1641

competitive substance and a solid phase coated with a quenching substance and having bound thereto, an analyte specific binding partner, to allow the analyte and the labeled competitive substance to competitively bind to the analyte specific binding partner, wherein the quenching substance suppresses the signal from the labeled competitive substance bound to the solid phase, exciting the sample so as to generate signal from unbound labeled competitive substance, and measuring the signal generated only from unbound labeled competitive substance in a defined volume of the liquid phase, thereby quantitatively or qualitatively determining the analyte without physically separating unbound and bound labeled competitive substance. Alternatively, a qualitative determination of the analyte can be obtained using the method when the quenching substance suppresses [only] at least some of the signal from the labeled competitive substance bound to the solid phase; 5) the relative skill of those in the art is high, yet 6) the state of the prior art has been shown to be unpredictable as evidenced by the fact that no prior art has been cited that disclose a method as claimed wherein the bound and unbound labeled components contained in the mixture are not physically separated and measured to provide both quantitative or qualitative determination of the analyte; and lastly 7) the claims broadly recite a method for quantitative or qualitative determination of an analyte by incubating a sample containing analyte with a labeled competitive substance and a solid phase coated with a quenching substance and having bound thereto, an analyte specific binding partner, to allow the analyte and the labeled competitive substance to competitively bind to the analyte specific binding partner, wherein the quenching substance suppresses at least some of the signal from

Art Unit: 1641

the labeled competitive substance bound to the solid phase, exciting the sample so as to generate signal from the labeled competitive substance, and measuring the signal generated from the labeled competitive substance, thereby quantitatively or qualitatively determining the analyte without physically separating unbound and bound labeled competitive substance; without any regard as to how the signal that determines the qualitative and quantitative measure of the analyte can be differentially generated and accurately measured without interference between bound and unbound components, since only at least some of the signal from the labeled competitive substance bound to the solid phase is suppressed by the quenching substance.

Therefore, it is maintained that one of ordinary skill in the art could not make and use the invention as claimed without undue experimentation.

Response to Arguments

5. Applicant's arguments with respect to claims 3-5, 10-16, 19, 21, 23, 33-36, and 42-44 have been considered but are moot in view of the new ground of rejection.

6. No claims are allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (571) 272-0820. The examiner can normally be reached on Monday, Tuesday, and Thursday, 7:00 AM to 4:30 PM.

Art Unit: 1641

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Gailene R. Gabel
Patent Examiner
Art Unit 1641
April 27, 2005